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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/780,394	02/17/2004	Stephen James Russell	07039-411002	1617

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EXAMINER	
NGUYEN, QUANG	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 09/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/780,394	RUSSELL ET AL.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 25 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 25 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/043,665.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 5/19/05.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S.D

DETAILED ACTION

Claim 25 is pending in the present application, and it is examined on the merits herein.

Sequence Compliance

The specification contains amino acid sequences that have not been assigned with SEQ ID NOs in either a paper sequence listing or in a CRF (see Fig. 8). It is also noted that the patentability of the presently claimed invention is not dependent on these amino acid sequences. **Failure to comply with the sequence rules will be deemed as non-responsive in the reply of this Office Action.**

Claim Objections

Claim 25 is objected to because of the term "said nucleic acid encoding said polypeptide can incorporate into the genome" is not grammatically correct. This is because the nucleic acid can't incorporate into the genome by itself, but rather in the form of a recombinant retroviral vector. Therefore, the phrase - - said nucleic acid encoding said polypeptide can be incorporated into the genome - - is more appropriate.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 25 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

An isolated retroviral packaging cell for transforming a quiescent cell with a nucleic acid encoding a polypeptide, said retroviral packaging cell comprising: (a) a retroviral vector, and (b) an exogenous nucleic acid encoding a growth factor, wherein said growth factor is displayed on the surface of said retroviral packaging cell, wherein said retroviral vector comprises said nucleic acid encoding said polypeptide, and wherein said growth factor displayed on the surface of said retroviral packaging cell can induce said quiescent cell to divide, so that said nucleic acid encoding said polypeptide can incorporate into the genome of said quiescent cell,

does not reasonably provide enablement for the same retroviral packaging cell ***in vivo***, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to **make and/or use** the invention commensurate in scope with these claims.

The factors to be considered in the determination of an enabling disclosure have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex parte Forman*, (230 USPQ 546 (Bd Pat. Appl & Unt, 1986); *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)).

As written, the instant claim encompasses both a retroviral packaging cell for transforming a quiescent cell with a nucleic acid encoding a polypeptide *in vitro* and *in*

vivo. When read in light of the specification, the sole purpose for the retroviral packaging cell *in vivo* is for medical treatment for a wide variety of disorders (see instant specification, at least page 1, lines 4-16; page 4, line 27 continues to line4 of page 5; page 8, line 25 continues to line 9 of page 9). There is no other disclosed use for the retroviral packaging cell *in vivo*. Please note that enablement requires the specification to teach how to make and **use** the claimed invention. The instant specification is not enabled for the present broadly claimed invention for the reasons discussed below.

1. The breadth of the claims

The instant claim encompasses both a retroviral packaging cell ***in vitro*** (or isolated) and ***in vivo*** for transforming **any quiescent cell** with a nucleic acid encoding **any polypeptide**, said retroviral packaging cell comprising: (a) a retroviral vector, and (b) an exogenous nucleic acid encoding **any growth factor**, wherein said growth factor is displayed on the surface of said retroviral packaging cell, wherein said retroviral vector comprises said nucleic acid encoding said polypeptide, and wherein said growth factor displayed on the surface of said retroviral packaging cell can induce said quiescent cell to divide, so that said nucleic acid encoding said polypeptide can incorporate into the genome of said quiescent cell

2. The state and the unpredictability of the prior art

The ***in vivo*** embodiment of the instant claim falls within the realm of gene therapy. At about the effective filing dates of the present application (9/28/95), the attainment of any therapeutic effect in general, for this instance the treatment of tumor cells or a tumor mass present within a mammal, through gene therapy was and remains

highly unpredictable as evidenced at least by the teachings of Dang et al. (Clin. Cancer Res. 5:471-474, 1999) and Romano et al. (Stem Cells 18:19-39, 2000). Dang et al. noted that further advancement in all fields such as gene delivery, gene expression and host immune manipulation is needed **to make gene therapy a reality**. Dang et al. also pointed out several factors limiting an effective human gene therapy, including sub-optimal vectors, the lack of a stable *in vivo* transgene expression, the adverse host immunological responses to the delivered vectors as well as an efficient gene delivery to target tissues or cells (last paragraph, col. 2, page 474). Even in 2000, Romano et al. still stated "The potential therapeutic applications of gene transfer technology are enormous. However, **the effectiveness of gene therapy programs is still questioned**", and "[d]espite the latest significant achievements reported in vector design, **it is not possible to predict to what extent gene therapeutic interventions will be effective in patients, and in what time frame**" (see abstract, col. 2).

Thus, it is apparent that the attainment of any therapeutic effect through the use of a retroviral packaging cell, particularly for transforming a quiescent cell with a nucleic acid encoding a polypeptide for medical treatment in a wide variety of disorders remains elusive in 2000, let alone at the effective filing date (9.28.1995) of the present application.

3. The amount of direction or guidance provided

The instant specification provides little or no guidance for a skilled artisan on how to obtain any contemplated therapeutic effect for medical treatment using a retroviral packaging cell for transforming any quiescent cell with a nucleic acid encoding any

polypeptide, particularly in light of the overall state and the unpredictability of the gene therapy art as already discussed above. For example, there is a complete lack of specific conditions or parameters used to transform any particular quiescent cell in any particular tissue or organ *in vivo* using the retroviral packaging cell of the present invention to yield the desired therapeutic effect. It is unclear which quiescent cell populations in which tissues or organs *in vivo*, and how are they brought into contact with the retroviral packaging cell in an effective manner so that the retroviral packaging cell can effectively induce the quiescent cells to divide and express the polypeptide in an effective amount that results in medical treatment for a wide variety of disorders. Especially, a quiescent cell encompasses a stem cell population that normally exists in minuscule amount among various other cell populations, and there is no means that the retroviral packaging cell can discriminate a stem cell population from non-stem cell populations. Since the prior art at the effective filing date of the present application does not provide such guidance, it is incumbent upon the present application to do so. With the lack of sufficient guidance provided by the present application, it would have required undue experimentation for a skilled artisan to make and use the instant broadly claimed invention.

4. Working example provided

There is an absence of an example demonstrating that any therapeutic effect has been attained or achieved *in vivo* using the retroviral packaging cell as claimed.

Accordingly, due to the lack of guidance provided by the specification regarding to the issues set forth above, the breadth of the claim, and the unpredictability of the art

the gene therapy art in general, it would have required undue experimentation for one skilled in the art to **make and use** the instant broadly claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 25 is rejected under 35 U.S.C. 102(b) as being anticipated by Paul et al. (WO 94/27643; IDS).

Paul et al disclose the preparation of retroviral packaging cells producing retroviral vectors bearing chimeric targeting proteins (CTPs) on their surfaces for introducing a heterologous gene into targeted cells, wherein chimeric targeting proteins comprised a ligand moiety that is a cytokine exhibiting cytokine effector activity to be used to modulate the growth, differentiation or other activity of the targeted cells (see Summary of the invention, particularly, page 6, lines 1-30). Paul et al further disclose a list of cytokines to be used in their invention, including interleukins (IL-1-13), GM-CSF, G-CSF, M-CSF, EPO, LIF, interferons, chemotactic factors, growth factors such as EGF, FGFs, PDGFs and others (page 14, lines 1-28). Paul et al specifically teach that a chimeric targeting protein generally comprises a signal peptide for insertion through the plasma membrane and is expressed in a packaging cell line such as LGPS (page 8, lines 10-22), and that cytokines may be either secreted from the cells that synthesize

them or they may be membrane-bound such as MGF and CSF (page 21, lines 18-21). Therefore, the cytokine having growth modulating activity will be displayed on the surface of the retroviral packaging cells. Additionally, Paul et al teach that the sequence encoding the CTP can be stably integrated into the genome of the packaging cell line or may be present on an extrachromosomal element such as a plasmid or other factor (page 33, lines 27-29), and a heterologous gene to be introduced into targeted cells include both positive and negative selectable genes (neo, HSV-I TK, HPRT, APRET) as well as numerous other foreign genes (page 36, line 5 continues to line 6 of page 37).

Accordingly, the retroviral packing cells of Paul et al meet all the limitation of the instant claim, and therefore the instant claim is anticipated by the reference. It should be noted that for a composition claim, its intended use is not given any patentably weight in light of the prior art. Furthermore, please, also note that where, as here, the claimed and prior art products are identical **or** substantially identical, or are produced by identical **or** substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke. Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, David Guzo, Ph.D., may be reached at (571) 272-0767, or SPE, Dave Nguyen, at (571) 272-0731.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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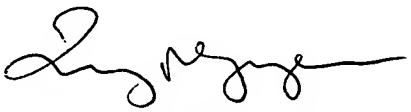

QUANG NGUYEN, PH.D
PATENT EXAMINER